

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) A method for generating a network of direct and indirect interaction partners of a disease-related (poly)peptide comprising the steps of
 - (a) contacting a selection of (poly)peptides suspected to contain one or several of said direct or indirect interaction partners with said disease-related (poly)peptides and optionally with known direct or indirect interaction partners of said disease-related (poly)peptide under conditions that allow the interaction between interaction partners to occur;
 - (b) detecting (poly)peptides that interact with said disease-related (poly)peptide or with said known direct or indirect interaction partners of said disease-related (poly)peptide;
 - (c) contacting (poly)peptides detected in step (b) with a selection of (poly)peptides suspected to contain one or several (poly)peptides interacting with said (poly)peptides detected in step (b) under conditions that allow the interaction between interaction partners to occur;
 - (d) detecting proteins that interact with said (poly)peptides detected in step (b);
 - (e) contacting said disease-related (poly)peptide and optionally said known direct or indirect interaction partners of said disease-related (poly)peptide, said (poly)peptides detected in steps (b) and (d) and a selection of proteins suspected to contain one or several (poly)peptides interacting with any of the afore mentioned (poly)peptides under conditions that allow the interaction between interaction partners to occur;
 - (f) detecting (poly)peptides that interact with said disease-related (poly)peptide and optionally said known direct or indirect interaction partners of said disease-related (poly)peptide or with said (poly)peptides identified in step (b) or (d); and
 - (g) generating a (poly)peptide-(poly)peptide interaction network of said disease-related (poly)peptide and optionally said known direct or indirect interaction partners of said disease-related (poly)peptide and said (poly)peptides identified in steps (b), (d) and (f).

2. (original) The method of claim 1, wherein said contacting step (e) is effected in an interaction mating two hybrid approach.

3. (currently amended) The method of claim 1 [[or 2]], said method comprising after step (d) and before step (e) the steps of:

(d') contacting (poly)peptides detected in step (d) with a selection of (poly)peptides suspected to contain one or several (poly)peptides interacting with said (poly)peptides detected in step (d) under conditions that allow the interaction between interaction partners to occur; and

(d'') detecting proteins that interact with said (poly)peptides detected in step (d').

4. (currently amended) The method of ~~any one of claims 1 to~~ claim 3, wherein said disease-related protein is a protein suspected of being a causative agent of a hereditary disease.

5. (currently amended) The method of ~~any one of claims 1 to~~ claim 4, wherein said disease-related protein is huntingtin and wherein said interaction partners are the interaction partners as shown in tables 6, 7 or 9.

6. (currently amended) The method of ~~any one of claims 1 to~~ claim 5, said method comprising the step of determining the nucleotide sequence of a nucleic acid molecule encoding a direct or indirect interaction partner of the disease related protein.

7. (currently amended) The method of ~~any one of claims 1 to~~ claim 6, wherein said selections of proteins are translated from a nucleic acid library.

8. (currently amended) The method of ~~any one of claims 1 to~~ claim 7, wherein said selection of proteins in step (a) and/or (c) and/or (d') and/or (e) is the same selection or a selection from the same source.

9. (currently amended) The method of ~~any one of claims 1 to~~ claim 7, wherein said selection of proteins in step (a) and/or (c) and/or (d') and/or (e) is a different selection or a selection from a different source.

10. (currently amended) The method of ~~any one of claims 1 to~~ claim 9, wherein said method is performed by contacting the proteins on an array.

11. (currently amended) The method of ~~any one of claims 1 to~~ claim 10, wherein said interactions are detected by using the yeast two-hybrid system.

12. (currently amended) The method of ~~any one of claims 1 to~~ claim 11, containing after step (b), (d), (d'') or (f) the additional steps of isolating a nucleic acid molecule with homology to said cDNA expressing the encoded protein and testing it for its activity as a modulator of huntingtin, wherein said nucleic acid molecule is DNA, or RNA, preferably cDNA, or genomic or synthetic DNA or mRNA.

13-19. (canceled).

20. (currently amended) A (poly)peptide comprising an amino acid sequence ~~encoded by a nucleic acid molecule of any one of claims 13 to 16, or which is chemically synthesized, or is obtainable from the host cell of claim 18, or which is obtainable by the method of claim 19 or which is obtainable from an in vitro translation system by expressing the nucleic acid molecule of any one of claims 13 to 16 or the vector of claim 17 of a protein listed in table 8.~~

21. (original) The (poly)peptide of claim 20 fused to a heterologous (poly)peptide.

22. (original) A protein complex comprising at least two proteins, wherein said at least two proteins are selected from the group of interaction partners listed in table 9.

23-24. (canceled)

25. (currently amended) A method of identifying whether a protein promotes huntingtin aggregation, comprising

- (a) transfecting a first cell with a nucleic acid molecule encoding a variant of the huntingtin protein or a fragment thereof capable of forming huntingtin aggregates;
- (b) co-transfected a second cell with
 - (i.) a nucleic acid molecule encoding a variant of the huntingtin protein or a fragment thereof capable of forming huntingtin aggregates; and
 - (ii.) a nucleic acid molecule encoding a candidate modulator protein identified by the ~~methods of any one of claims 1 to 12~~ method of claim 1 or a nucleic acid molecule encoding a modulator protein selected from table 6 or table 7;
- (c) expressing the proteins encoded by the transfected nucleic acid molecule of (a) and (b);
- (d) isolating insoluble aggregates of huntingtin from the transfected cell of (a) and (b); and
- (e) determining the amount of insoluble huntingtin aggregates from the transfected cell of (a) and (b)

wherein an increased amount of huntingtin aggregates isolated from the transfected cells of (b) in comparison with the amount of huntingtin aggregates isolated from the transfected cells of (a) is indicative of a protein's activity as an enhancer of huntingtin aggregation.

26. (currently amended) A method of identifying whether a protein inhibits huntingtin aggregation, comprising

- (a) transfecting a first cell with a nucleic acid molecule encoding a variant of the huntingtin protein or a fragment thereof capable of forming huntingtin aggregates;
- (b) co-transfected a second cell with
 - (i.) a nucleic acid molecule encoding a variant of the huntingtin protein or a fragment thereof capable of forming huntingtin aggregates ; and

(ii.) a nucleic acid molecule encoding a candidate modulator protein identified by the ~~methods of any one of claims 1 to 12~~ method of claim 1 or a nucleic acid molecule encoding a modulator protein selected from table 6 or table 7;

- (c) expressing the proteins encoded by the transfected nucleic acid molecule of (a) and (b);
- (d) isolating insoluble aggregates of huntingtin from the transfected cell of (a) and (b); and
- (e) determining the amount of insoluble huntingtin aggregates from the transfected cell of (a) and (b)

wherein a reduced amount of huntingtin aggregates isolated from the transfected cells of (b) in comparison with the amount of huntingtin aggregates isolated from the transfected cells of (a) is indicative of a protein's activity as an inhibitor of huntingtin aggregation.

27. (currently amended) The method of claim [[25 or]] 26, wherein prior to step (d) the cells are treated with an ionic detergent.

28. (currently amended) The method of ~~any one of claims 25 to~~ claim 27, wherein the huntingtin aggregates are filtered or transferred onto a membrane.

29-31. (canceled)

32. (original) A method of diagnosing Huntington's disease in a biological sample comprising the steps of

- (a) contacting the sample with an antibody specific for a protein of table 6 or 7 or an antibody specific for the protein complex of claim 22; and
 - (b) detecting binding of the antibody to a protein complex,
- wherein the detection of binding is indicative of Huntington's disease or of a predisposition to develop Huntington's disease.

33-36. (canceled)